News and Resources from the National Institutes of Health

Digestive Diseases
NEWS
National Digestive Diseases Information Clearinghouse
Winter 2009

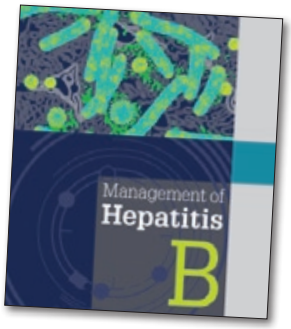
NIH Hosts Consensus Conference on Hepatitis B Management

At a recent consensus development conference, a 12-member panel of experts, tasked by the National Institutes of Health (NIH) to identify strategies for managing hepatitis B, recommended studies to assess the long-term effectiveness of current treatments and urged routine screening programs for immigrants arriving from countries where the hepatitis B prevalence rate is greater than 2 percent.

"While there is little controversy about the use of the hepatitis B vaccine and other preventive measures against this disease, there is considerable controversy about its treatment," said National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Director Griffin P. Rodgers, M.D., M.A.C.P. "This controversy is really the reason for and the focus of this consensus development conference."

The conference was part of the NIH Consensus Development Program, which was established in 1977 to review controversial topics in medicine and public health in an unbiased, impartial manner. At the conference's conclusion, the consensus panel issued a 25-page consensus statement based on a systematic review of the literature by the U.S. Agency for Healthcare Research and Quality (AHRQ) and expert testimony at the conference.

The panel reported that more than 400 million people worldwide are living with chronic hepatitis B, contributing to more than 500,000 deaths per year. In the United States, more than 1 million people have chronic hepatitis B, with hepatitis B-related hospitalization costs running more than $1 billion annually. Between 47 and 70 percent of U.S. residents with chronic hepatitis B were born outside the United States.



Which people should be treated, according to the panel, depends on the phase of the disease and other factors, including age, pregnancy status, sex, concomitant immunosuppressive or cancer therapies, coinfection with other forms of viral

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NIDDK
National Institute of Diabetes and Digestive and Kidney Diseases

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Griffin P. Rodgers, M.D., M.A.C.P.
Director, NIDDK

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hepatitis or with HIV, hepatitis B viral genotype, family history of hepatocellular carcinoma, and alcohol abuse.

The panel concluded that patients with acute liver failure, decompensated cirrhosis, or compensated cirrhosis and increased risk of developing complications should be treated with antiviral therapy. Therapy may be indicated in other cases due to a combination of disease activity and other factors, such as age.

The panel cited data showing that the odds of spontaneous clearance of the virus decreases after about age 40, thus increasing the likelihood of hepatitis B-related complications. If, by this age, a patient shows signs of being immune active—with high alanine transaminase levels and positive for the hepatitis B antigen—therapy to slow disease progression should be considered. Therapy is not indicated for patients in the immune tolerant or inactive carrier phases.

Hepatitis B is a liver disease spread through contact with infected blood or body fluids. Although the rate of new infections in the United States has dropped precipitously with the advent of vaccines, hepatitis B-related liver damage and hepatocellular carcinoma continue to be significant health problems.

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NIH Consensus Panel Addresses Major Questions about Hepatitis B

The National Institutes of Health (NIH) hepatitis B consensus panel addressed six major questions when it convened October 20–22, 2008.

- What is the current burden of hepatitis B?
- What is the natural history of hepatitis B?
- What are the benefits and risks of current hepatitis B therapies?
- Which people with hepatitis B should be treated?
- What measures are appropriate to monitor therapy and assess outcomes?
- What are the greatest needs and opportunities for future hepatitis B research?

To address these questions, the panel considered a systematic review of the literature by the U.S. Agency for Healthcare Research and Quality and expert testimony by hepatitis B researchers and clinicians at the conference.

Digestive Diseases
NEWS

Digestive Diseases News, an email newsletter, is sent to subscribers by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about digestive diseases, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

If you would like to subscribe, go to *http://catalog.niddk.nih.gov/newsletter.cfm*. You can read or download a PDF version of the newsletter at *http://digestive.niddk.nih.gov/about/newsletter.htm*.

Executive Editor: Stephen P. James, M.D.

Dr. James is the director of the Division of Digestive Diseases and Nutrition within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). As director, Dr. James oversees planning, implementation, and evaluation of a national research effort focused on gastrointestinal, pancreatic, hepatobiliary, and nutrition diseases and conditions. Before joining the NIDDK in 2001, Dr. James directed the division of gastroenterology at the University of Maryland's School of Medicine for 10 years.

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People at greatest risk of hepatitis B are those born to infected mothers. Unless vaccinated at birth, the likelihood these people will develop chronic hepatitis B years later is greater than 90 percent. U.S. residents who were born in hepatitis B-endemic areas of the world are at greatest risk for chronic disease. Unvaccinated, U.S.-born populations at greatest risk include intravenous drug users and men who have sex with men.

Future Research

The greatest needs and opportunities for future hepatitis B research cited by the panel include

- multinational, population-based prospective cohort studies to further define the natural history of hepatitis B
- large, multicenter, placebo-controlled clinical trials of mono- and combination therapies
- elucidation of the role of viral replication in host response and carcinogenesis
- risk and benefit assessment of antiviral therapy
- studies of the quantitative and qualitative characteristics of the host immune response to chronic hepatitis B infection
- evaluation of the risks and benefits of screening for hepatocellular carcinoma in people with chronic hepatitis B

No optimal approach exists for monitoring the progression of hepatitis B and assessing outcomes, according to the panel. Hepatitis B can seemingly enter the inactive phase—measured by diminished viral load and the disappearance of viral antigen—only to resurface later for unknown reasons. In many cases, liver damage continues after all other signs point to inactive disease, which is often the case in people who were infected at birth. The panel suggested expanding research to improve current disease monitoring algorithms.

The panel also recommended more research to unveil factors affecting disease progression and carcinogenesis. The panel recognized the NIDDK's plans to launch the Hepatitis B Clinical Research Network—an effort to accelerate clinical and translational research toward effective and practical hepatitis B therapies. The consensus statement recommendations are expected to inform the network's research agenda.

The panel's consensus statement—an independent report and not a policy statement of the NIH or the Federal Government—was

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Three Phases of Hepatitis B Infection

The National Institutes of Health hepatitis B consensus panel recognized three distinct phases that may occur during the natural history of hepatitis B infection:

- the immune tolerant phase, when the virus is present but the body's immune system is not generating antibodies and liver inflammation is not detectable
- the immune active phase—associated with liver inflammation, liver damage, and possibly hepatocellular carcinoma—when the body is actively fighting off the virus
- the inactive carrier phase, when the virus is controlled by the immune system and liver damage stops progressing

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published in the January 20, 2008, issue of *Annals of Internal Medicine.* The consensus statement, AHRQ literature review, and full webcast of the consensus conference are available at *www.consensus.nih.gov/2008/2008HepatitisBCDC120main.htm.*

The NIH has conducted more than 100 consensus development conferences addressing a wide range of issues. Information about the NIH Consensus Development Program is available at *www.consensus.nih.gov/forthemedia.htm.*

The NIDDK has health information about hepatitis B at *www.digestive.niddk.nih.gov/ddiseases/topics/hepatitis.asp.* ■

Current Approved Chronic Hepatitis B Therapies

Preventing the progression of cirrhosis, liver failure, and hepatocellular carcinoma is the primary goal of chronic hepatitis B treatment. Although seven hepatitis B therapies are approved in the United States, the National Institutes of Health hepatitis B consensus panel recognized that none have been demonstrated to improve primary clinical outcomes, such as the prevention of cancer or liver failure. Instead, effectiveness has been extrapolated from surrogate outcomes based on changes in viral load, the presence or absence of hepatitis B antigens and antibodies, liver function tests, and liver histology.

Therapies approved by the U.S. Food and Drug Administration for chronic hepatitis B include

- interferon-alpha
- peginterferon-alpha
- lamivudine
- adefovir
- entecavir
- tenofovir
- telbivudine

"We know these therapies have positive effects on indicators such as viral load, but further controlled trials are needed to substantiate that these agents prevent disease progression to liver failure, cancer, or death," explained Consensus Panel Chair Michael F. Sorrell, M.D., professor of medicine at the University of Nebraska Medical Center. The panel recommended long-term, placebo-controlled trials of both mono- and combination therapies to test long-term effectiveness.

Long-term Peginterferon Therapy for Hepatitis C Treatment Reduces Viral Levels but Liver Damage Continues

Treating patients who have chronic hepatitis C and advanced liver disease with long-term peginterferon significantly decreases liver enzymes, viral levels, and liver inflammation, but treatment does not slow or prevent the progression of serious liver disease, according to a study funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

"The results from HALT-C show without question that maintenance therapy with peginterferon does not prevent progression of liver disease among patients who have failed prior treatments."

James Everhart, M.D.
Project Scientist, HALT-C, Division of Digestive Diseases and Nutrition, NIDDK

The study's findings come from the clinical trial Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) and are reported in the December 4 issue of *The New England Journal of Medicine*. Additional support for HALT-C comes from Hoffmann-La Roche, Inc.

"The results from HALT-C show without question that maintenance therapy with peginterferon does not prevent progression of liver disease among patients who have failed prior treatments," said James Everhart, M.D., project scientist for HALT-C in the NIDDK's Division of Digestive Diseases and Nutrition. "These findings heighten the incentive to develop more effective drugs for patients with severe liver disease due to hepatitis C."

Peginterferon therapy for up to 48 weeks is standard for chronic hepatitis C. Nonresponders—patients who do not have a sustained response to initial therapy—are given the drug over a longer time, based on studies showing this approach suppresses viral and enzyme levels even if the virus is not completely eliminated. However, it was not known if long-term maintenance therapy would improve important clinical outcomes such as liver damage and death.

HALT-C, a randomized, multicenter trial of 1,050 nonresponders, tested whether long-term treatment with peginterferon alfa-2a (Pegasys) would reduce the development of cirrhosis, liver cancer, or liver failure. The 517 patients randomized to the treatment group received 90 micrograms of peginterferon in weekly injections for 3.5 years. The 533 patients in the control group underwent the same follow-up and care as the treated patients, including liver biopsies, quarterly clinic visits, and blood tests but did not receive peginterferon injections. All patients had advanced liver fibrosis, a gradual scarring of the liver that puts patients at risk for progressive liver disease and liver failure.

The outcomes studied in HALT-C were death, liver cancer, or liver failure and, for those who did not have cirrhosis initially, the development of cirrhosis. At the end of the study, 34.1 percent of the treatment group and 33.8 percent of the control group had experienced at least one outcome. Patients in the treatment group had significantly lower blood levels of the hepatitis C virus and improvement in liver inflammation. However, no major difference existed in rates of any of the primary outcomes between the groups.

Among treated patients, 17 percent stopped peginterferon after 18 months and 30 percent

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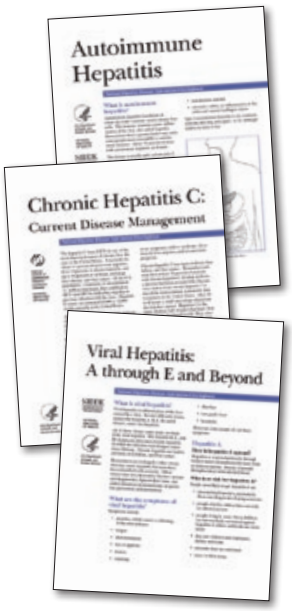
stopped the drug after 2 years. Infections and musculoskeletal or digestive problems were the most common reasons for stopping the drug.

Important Step

Looking into how maintenance therapy works in nonresponders is an important step, according to HALT-C Study Chair and Principal Investigator Adrian M. Di Bisceglie, M.D., professor of internal medicine at Saint Louis University School of Medicine. "Patients should not receive interferon as maintenance therapy for chronic hepatitis C. However, we can build on what was learned in HALT-C to identify better treatments that may delay or prevent liver damage in patients with advanced disease."



The hepatitis C virus infects more than 100 million people worldwide and as many as 4 million people in the United States. Hepatitis C ranks with alcohol abuse as the most common cause of chronic liver disease and leads to about 1,000 liver transplants in the United States each year. The best current antiviral therapy of peginterferon given by injection in combination with oral ribavirin for about 6 months to a year eliminates the virus in about 50 percent of infected patients.

The NIDDK has fact sheets and easy-to-read booklets about hepatitis C at *www.digestive.niddk.nih.gov/ddiseases/topics/hepatitis.asp.*

For information about NIDDK liver disease research, see *www2.niddk.nih.gov/AboutNIDDK/ResearchAndPlanning/Liver_Disease/Action_Plan_For_Liver_Disease_Intro.htm.*

For more information about the HALT-C trial, see *www.niddk.nih.gov/patient/halt-c/halt-c.htm.* ■

The following researchers and clinical centers conducted the HALT-C study:

- Jules L. Dienstag, M.D., Massachusetts General Hospital and Harvard Medical School, Boston
- Adrian M. Di Bisceglie, M.D. (study chair), Saint Louis University School of Medicine
- Anna S. Lok, M.D., University of Michigan Medical Center, Ann Arbor
- Gyongyi Szabo, M.D., Ph.D., University of Massachusetts, Worcester
- Timothy R. Morgan, M.D., University of California, Irvine, and VA Long Beach Healthcare System, Long Beach, CA
- Gregory T. Everson, M.D., University of Colorado Health Sciences Center, Denver
- Herbert L. Bonkovsky, M.D., University of Connecticut Health Center, Farmington
- Karen L. Lindsay, M.D., Keck School of Medicine, University of Southern California, Los Angeles
- William M. Lee, M.D., University of Texas Southwestern Medical Center, Dallas
- Mitchell L. Shiffman, M.D., Virginia Commonwealth University Medical Center, Richmond
- Chihiro Morishima, M.D., and David Gretch, M.D., Ph.D., University of Washington, Seattle
- Kristin K. Snow, Sc.D., New England Research Institutes, Watertown, MA
- Marc G. Ghany, M.D., Liver Disease Research Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD

NIDDK Hosts Workshop on Drug-induced Liver Injury

An international group of scientists met December 1–2, 2008, at the National Institutes of Health in Bethesda, MD, to help develop a standardized approach to diagnosing and determining the severity of drug-induced liver injury (DILI). The workshop, organized by the Liver Disease Research Branch of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), was designed to foster discussion among DILI experts and stimulate international collaboration.

"Predicting those at risk for drug-induced liver injury is a critical issue."

Neil Kaplowitz, M.D.
Director, Research Center for Liver Diseases, University of Southern California, Los Angeles

Recognizing DILI is a challenge, as it mimics all forms of acute and chronic liver disease, according to Neil Kaplowitz, M.D., director of the Research Center for Liver Diseases at the University of Southern California, Los Angeles. DILI-specific biomarkers have yet to be found. DILI is often reversible, but failure to recognize it can quickly lead to serious health complications, even death. "Predicting those at risk for drug-induced liver injury is a critical issue," Kaplowitz said.

DILI is the leading cause of acute liver failure in the United States and is becoming an increasingly important health concern as more people take prescription, over-the-counter, and herbal medications. Liver injury is also the major reason drugs fail to win approval from the U.S. Food and Drug Administration.

Although the incidence of DILI is unclear—relying on spontaneous reporting from health care professionals—serious adverse drug reactions account for about 4.7 percent of hospital admissions in the United States. While reactions to specific drugs are thought to be rare, according to Einar Bjornsson, M.D., Ph.D., professor of gastroenterology and hepatology at the Sahlgrenska Hospital, Gothenburg, Sweden, "there is a huge underreporting of adverse reactions in general," suggesting cases of DILI may also be much higher. Collectively, DILI cases represent a significant health problem, much of which is preventable.

Standardizing DILI Assessment

The Roussel Uclaf Causality Assessment Method (RUCAM) is the most widely known instrument for assessing DILI. Using RUCAM, a health care provider derives a score indicating the likelihood that liver injury is due to a specific medication, based on a patient's clinical, biological, serological, and radiologic features. RUCAM, however, has not been widely adopted in the clinic.

"Components of RUCAM are broken," said Paul Watkins, M.D., director of the Hamner-UNC Center for Drug Safety Sciences, Research Triangle Park, NC, who co-chaired a session about issues related to causality assessment.

RUCAM's shortcomings include ambiguous definitions, lack of reproducibility, and components that are not supported by data, according to Maribel Lucena, M.D., professor of clinical pharmacology at the University of Malaga in Spain. Above all, RUCAM's complexity limits

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its practical use. A show of hands at the workshop revealed only about 10 percent of participants use RUCAM.

Despite its shortcomings, many at the meeting believe it is better to fix RUCAM than start from scratch. "What we'd like to have is a computer [program] that you could put the data into to calculate the RUCAM score," said Jay Hoofnagle, M.D., director of the NIDDK's Liver Disease Research Branch. Such a program, according to Hoofnagle, would facilitate testing and deciding which components to include in a revised RUCAM.

The DILI Network

The impetus behind the workshop was the NIDDK's DILI Network (DILIN), initiated in 2003 to advance understanding and research into DILI. The DILIN, said Leonard Seeff, M.D., senior scientist at the NIDDK's Liver Disease Research Branch, provides a stimulus and resource for research and clinical investigation of all forms of DILI.

The DILIN, a collaboration among investigators at nine clinical study centers plus one data coordination center and the NIDDK, is sponsoring retrospective and prospective DILI studies with corresponding patient registries. Both studies are enabling investigators to examine clinical, genetic, immunological, and environmental risk factors in slightly different ways.

The retrospective study is unraveling why certain drugs elicit DILI in only a slim minority of people. The study is examining four specific drugs: isoniazid (INH), phenytoin (Dilantin), clavulanic acid/amoxicillin (Augmentin), and valproic acid (Depakote). DILI signs and symptoms resulting from these agents are relatively well-defined, providing the opportunity to explore common environmental and genetic contributors. The retrospective registry houses clinical details about DILI episodes along with DNA and blood samples.

Member Organizations of the Drug-Induced Liver Injury Network

- Duke University, Durham, NC (Data Coordinating Center)
- Indiana University, Indianapolis
- Mayo Clinic, Rochester, MN
- Thomas Jefferson University, Philadelphia
- University of California, San Francisco
- University of Michigan, Ann Arbor
- University of North Carolina, Chapel Hill
- University of Pennsylvania, Philadelphia
- University of Southern California, Los Angeles
- University of Texas Southwestern, Dallas

The more ambitious prospective study is allowing scientists to study idiosyncratic DILI during the initial phase: from first presentation onward. Included are cases of DILI caused by all prescription and over-the-counter medications, herbals, and nutritional supplements. Once enrolled, patients are followed for a minimum of 6 months but possibly as long as 20 years. Controls—volunteers with similar drug exposure but no DILI—will be enrolled for comparison.

Improving instruments for causality assessment is one of the primary objectives of the prospective study. Three DILIN investigators review the clinical, diagnostic, and laboratory data for each suspected DILI case and then assign causality, first by expert opinion and then by RUCAM.

The DILIN worked out a scoring system similar to RUCAM. Like RUCAM, the expert opinion method derives a score indicating the likelihood that DILI is due to a specific medication. Scores range from 1 (definite) to 5 (highly unlikely). To put the scores into context, the DILIN assigned

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descriptive terms and percentages to the scores. For example, a score of 1 is defined by the DILIN as "Liver injury is typical for the drug or herbal product. The evidence for causality is beyond reasonable doubt," with a 95 percent likelihood that the drug in question is responsible.

A comparison of the two causality assessment methods showed the DILIN expert opinion method had less variability and that RUCAM tended to underestimate drug injury association, according to Don Rockey, M.D., professor and chief of the division of digestive and liver diseases at the University of Texas Southwestern Medical Center. He said that although the expert opinion method cannot be applied broadly, as too few hepatologists exist relative to the number of suspected cases, he believes study data will help develop a more generalizable and quantitative assessment method.

For information about the NIDDK's Liver Disease Research Branch, go to *www2.niddk.nih.gov/Research/ScientificAreas/Liver/DILD.htm.*

For more information about the DILIN, go to *http://dilin.dcri.duke.edu.* ■

LiverTox: A New Database for DILI

Plans for LiverTox—a new website featuring general information about drug-induced liver injury (DILI), specific information about drugs, and a platform for user input—were discussed at the DILI workshop.

"LiverTox will be a multilayered, informational, and interactive website with comprehensive information on drug- and herbal medication-induced liver injury available to physicians and the general public without charge," said Jay Hoofnagle, M.D., director of the National Institute of Diabetes and Digestive and Kidney Diseases' (NIDDK's) Liver Disease Research Branch, who introduced the website. James Knoben, Pharm.D., M.P.H., a consultant at the National Library of Medicine (NLM), demonstrated the new website to workshop participants.

A collaboration between the NLM and the NIDDK's Liver Disease Research Branch, LiverTox is intended to be a gateway for general care providers, specialists, and the general public to both retrieve and contribute information. A major component of the website is a reference database cataloging information about the hepatotoxicity of specific medications and supplements, eventually holding as many as 1,000 records.

LiverTox is currently available to a few select experts for review during the development process. A limited version of the website is scheduled to become available to the public as early as Fall 2009.

Zerhouni Ends Tenure as NIH Director

Deputy Director Kington Steps in as Acting Director

Elias A. Zerhouni, M.D., a physician-scientist and world-renowned leader in radiology research, ended his tenure as director of the National Institutes of Health (NIH). From May 2002 through October 2008, Zerhouni led the agency through a challenging period that required innovative solutions to transform basic and clinical research into tangible benefits for patients and their families.

"I have had the privilege of leading one of the greatest institutions in the world for six-and-a-half years."

Elias A. Zerhouni, M.D.

Zerhouni plans to pursue writing projects and explore other professional opportunities.

"I have had the privilege of leading one of the greatest institutions in the world for six-and-a-half years," Zerhouni said. "NIH's strength comes from the extraordinary commitment and excellence of its people in serving a noble mission. It also comes from the nation's scientific community, whose discoveries alleviate the suffering of patients throughout the world."

NIH Roadmap

The hallmark of Zerhouni's tenure is the NIH Roadmap for Medical Research, launched in 2003 after extensive consultations with the scientific community. The NIH Roadmap brought together the NIH's 27 Institutes and Centers to fund compelling research initiatives that could have a major impact on science but that no single Institute could tackle alone.

Reaching out to the Public

Under Zerhouni's leadership, the NIH reached out to the public in an unprecedented way with the communication of science-based health information and scientific results. He led efforts to make the incomparable resources of the NIH and its grantees accessible to the public. Key to these efforts are the health education programs across the agency, including the development of materials for people who have literacy, language, or access barriers.

The NIH is part of the U.S. Department of Health and Human Services and is the nation's premiere biomedical research agency. The agency has more than 18,000 employees and a fiscal year 2008 budget of $29.5 billion. It supports more than 325,000 research personnel at more than 3,100 institutions throughout the United States and around the world.

Raynard S. Kington, M.D., Ph.D., NIH deputy director under Zerhouni, will serve as acting director until a permanent director is appointed by President Obama. ■

Featured in the NIDDK Reference Collection

Cooking for Crohn's and Colitis

How to Cook for Crohn's and Colitis: More than 200 Healthy, Delicious Recipes the Whole Family Will Love provides information and recipes for people with inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis. The introductory material shares the author's story of being diagnosed with Crohn's disease, basic information about the symptoms and complications of IBD, treatments including surgery and medications, nutritional therapy, the role of psychosocial factors including stress and depression, lactose intolerance, the role of dietary fats and fiber, probiotics, and components of a healthy diet. The cookbook presents recipes in 11 categories: appetizers, soups, salads and salad dressings, sandwiches, savory and sweet breads, beef and pork entrees, poultry entrees, fish and seafood entrees, pasta and sauces, side dishes and condiments, and sweets. Each recipe includes an ingredients list, preparation instructions, and suggested variations. The cookbook concludes with a list of suggested readings, Internet resources, and a subjects and recipes index. The 224-page book is $14.63 from Sourcebooks, Inc., 1935 Brookdale Road, Suite 139, Naperville, IL 60563, 1–800–432–7444, 630–961–2168 (fax), *salesorders@sourcebooks.com, www.sourcebooks.com.*

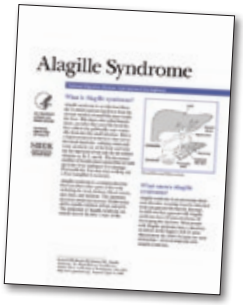
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection is a free, online database that helps health care professionals, health educators, patients, and the general public find educational materials not typically referenced in most databases. The NIDDK does not control or endorse the information contained in this collection; the information is provided as a convenience to our visitors.

To find more resources about digestive diseases, visit *www.catalog.niddk.nih.gov/resources.*

Additional Resources

New Publications

Alagille syndrome is an inherited disorder in which the liver contains too few hepatic ducts. Bile builds up in the liver, which can lead to liver damage and possibly liver failure. A complex disorder, Alagille syndrome affects other body systems, including the heart, kidneys, blood vessels, eyes, face, and skeleton. Alagille syndrome occurs in about one in every 70,000 births, with symptoms usually appearing in the first 2 years of life. The National Digestive Diseases Information Clearinghouse's (NDDIC) new fact sheet, *Alagille Syndrome,* provides consumers and health care providers with useful information about the causes, symptoms, diagnosis, treatment, and long-term outlook for people with Alagille syndrome.



This new fact sheet is available at *www.digestive.niddk.nih.gov.*

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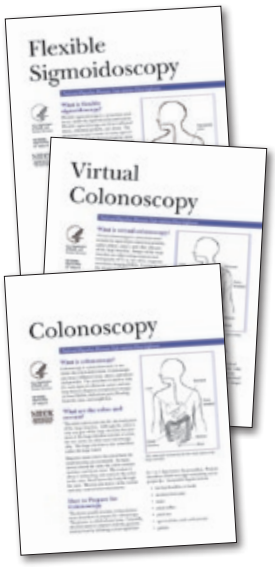

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Updated Fact Sheets

The NDDIC has updated the following fact sheets:

- *Abdominal Adhesions*
- *Appendicitis*
- *Cirrhosis*
- *Colonoscopy*
- *Cyclic Vomiting Syndrome*
- *Flexible Sigmoidoscopy*
- *Indigestion*
- *Inguinal Hernia*
- *Irritable Bowel Syndrome in Children*
- *Ménétrier Disease*
- *Primary Biliary Cirrhosis*
- *Virtual Colonoscopy*

These publications are available at *www.digestive.niddk.nih.gov.*

Information about Pediatric Digestive Diseases: CDHNF and NASPGHAN

Educational resources about gastrointestinal, liver, and nutritional issues for children and their families are available through the Children's Digestive Health and Nutrition Foundation (CDHNF) and its partner organization, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN).

The CDHNF's Digestive Health for Life Campaigns aim to improve the quality of life and health outcomes for children suffering from four specific disorders: celiac disease, eosinophilic esophagitis, inflammatory bowel disease, and gastroesophageal reflux disease. Information about the symptoms, diagnosis, management, and medical therapy for these disorders is available at the CDHNF's website, *www.cdhnf.org.*

Titles available from the NASPGHAN include *Alpha-1-Antitrypsin Deficiency, Encopresis, Nutrition and Cystic Fibrosis, Fundoplication,* and many more. Most publications are available in English, French, Portuguese, and Spanish. To find a local pediatric gastroenterologist, obtain more information, or download these fact sheets, go to *www.naspghan.org.* ■

Upcoming Meetings, Workshops, and Conferences

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will exhibit at the following upcoming events:

American Association for the Study of Liver Diseases 13th International Symposium on Viral Hepatitis and Liver Disease

March 20–24 in Washington, D.C.
For more information, go to *www.isvhld2009.org.*

Society of Gastroenterology Nurses and Associates Annual Course

May 15–20 in St. Louis.
For more information, go to *www.sgna.org/Education/events/AnnualCourse/2009/registration09.cfm.*

American Academy of Physician Assistants Annual Conference

May 23–28 in San Diego.
For more information, go to *www.aapa.org/annual-conf/sandiego09/index.php.*

Digestive Disease Week

May 30–June 4 in Chicago.
For more information, go to *www.ddw.org/wmspage.cfm?parm1=679.*

NIDDK Organ Smooth Muscle: Development, Physiology, and Pathology

The NIDDK announces a 2-day workshop about the development, physiology, and pathology of organ smooth muscle. The workshop will be held at the National Institutes of Health Neuroscience Building in Rockville, MD, March 24–25, 2009, and will address current research about the biology of smooth muscle in organs and organ systems, as well as future smooth muscle research needs. The workshop will bring together investigators working on a variety of systems to stimulate discussion about research for future therapies to address organ dysfunction related to altered smooth muscle biology. For more information about the workshop, go to *www3.niddk.nih.gov/fund/other/smoothmuscle.* ■

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